

Monitoring effect of antiangiogenic treatments by DCE-US

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New treatments based on antiangiogenic substances are developed in order to destroy tumor vessels and are the object of promising clinical research for cancer treatment. Considering the large number of new targeted drugs under development, there is a great need for early reliable imaging indicators of tumour responses, and identification of a recommended modality of drug administration to guide further steps in the clinical development. The response rate remains the best objective parameter of efficacy of the treatments tested in Phase 1, 2, or 3 but this parameter is obtained very late in the clinical development, while the effect on the tumour must be determined as soon as possible in order to optimise the schedule and the dose to be recommended for the late clinical development stage. The early functional evaluation of new treatments is a main goal.

At present, technical advances in DCE-ultrasonography using bolus contrast agent and perfusion software allow the detection of microvascularization and perfusion for superficial and deep malignant tumors. Thus, it becomes possible to early evaluate the efficiency of antiangiogenic or anti-vascular molecules. Treatment response can be early predicted according to modifications of this vascularization before any volume modification. The acquisition of raw linear data affords the precise quantification (peak intensity, time to peak intensity, slope of wash-in, and area under the curve...) of the perfusion after contrast uptake curves modelization, in particular using time tracking of region of interest. The results will be focused on different treatments and several tumoral types including colon cancer. Reduction in tumor vascularization can easily be detected in responders after 1 or 2 weeks and is correlated with progression-free survival and overall survival in RCC or HCC.

DCE-US is supported by the French National Cancer Institute (INCa), which is currently studying the technique in metastatic breast cancer, melanoma, colon cancer, gastrointestinal stromal tumors and renal cell carcinoma, as well as in primary hepatocellular carcinoma, to establish the optimal perfusion parameters and timing for quantitative anticancer efficacy assessments. 539 patients (including 67 metastatic colon cancer) are included in 19 centers and the preliminary results on 400 patients including (45 metastatic colon cancer) with 1096 DCE-US demonstrated that AUC could be a robust parameter to predict response.

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Clin Cancer Res. 2010 Feb 15;16(4):1216-25